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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,009	03/24/2005	Kenji Soejima	081356-0237	4640

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,009	SOEJIMA ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-44* is/are pending in the application.

4a) Of the above claim(s) *39-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 37* is/are rejected.

7)☒ Claim(s) *35, 37 and 38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice To Comply* .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/14/2008, is acknowledged.

2. Claims 34-44 are pending.

3. Claims 39-43 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 34-38 are under consideration in the instant application as they read on an antibody against a protein or peptide of ADAMST-13 and SEQ ID NO: 1 as the species.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. The specification has described several amino acid sequences that each must have a sequence identifier.

The specification discloses the following sequences RQRR and HEXXHXXGXXHD (page 2, last ¶) and RGDS on page 3 (top ¶) that fail to comply with the sequence rule. Applicant is reminded of the sequence rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules. Correction is required.

6. Claims 35 and 37 are objected to for the following informalities:

A. The recitation "FERM BP-817**S**" should be "FERM BP-817**5**" (in claim 35).
B. The "WH2-22-**I**A" should be "WH2-22-**1**A" (in claim 35).
C. The "PEP4-**S**B-**I**" is misspelled, the correct spelling is "PEP4-**5**B-**1**" (in claim 35).
D. All the hybridomas "**0**8483", "BP-**0**8484", "BP-**0**8485", "BP-**0**8474" and "BP-**0**8475" are missing the "0" before "84XX" (in claims 35 and 37).
E. The "WH2-22-1" in claim 37, should be "WH2-22-1A".
F. The "BP-848**S**" in claim 37, should be "BP-848**5**".
G. The "Pep4-5B-**I**" in claim 37, should be "Pep-5B-**1**".

7. The Bent declaration in conjunction with the FERM deposit information, filed 7/14/08 are sufficient to overcome the previous rejection of the instant claims based upon the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

8. The following new ground of rejections necessitated by the amendment submitted 7/14/08.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) "the amino acid sequence constituting ADAMTS-13" in claim 34, implies representative of *any member* of a genus that is "represented by" the SEQ ID NO: 1. Such language fails to establish the metes and bounds of amino acid sequence encompassed by the instant claim language; therefore the claim is indefinite.

B) The recitation "and Tsp1-8 domain" in claim 34 is ambiguous. The conjunction "or" should be used when listing the ADAMTS-13 "portion" species.

C) The recitation "any of the disintegrin-like domain" in claim 34 is ambiguous. It is not clear how many disintegrin-like domain the ADAMTS-13 has.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 36 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a monoclonal produced by the hybridoma listed in claim 35, does not reasonably provide enablement for a "pharmaceutical composition" of claim 36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 1/15/2008.

Applicant's arguments, filed 7/14/08, have been fully considered, but have not been found convincing.

Applicant did not address the rejection with respect to the intended *in vivo* use of the claimed antibodies "pharmaceutical composition". Accordingly the rejection is maintained for reasons of records. The rejection is reiterated herein:

At issue is whether or not the claimed composition would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence

of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al (Biochimica et Biophysica Acta 1343:316–326, 1997).

Liu et al teach the monoclonal antibody 134B29 which binds to RGDS (see page 318, 1st col., line 7 in particular). RGDS is located at position 498-501 of ADAMTS-13. Accordingly, the anti-RGDS monoclonal antibody of Liu et al would recognize the Cys-rich region to the spacer domain of the ADAMTS-13.

The reference teachings anticipate the claimed invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zheng et al in view of Campbell.

Zheng et al teach the use of anti-VWFCP antibodies to assess VWFCP deficiency with TTP (see page 41062 last ¶ in particular). Referenced VWFCP of Fig. 1 shares 100% sequence homology with claimed SEQ ID NO:1. Further, Zheng et al teach identified VWFCP as a member of the ADAMTS family of metalloproteases and designated ADAMTS13. VWFCP consist of 1427 amino acid residues and has a disintegrin like domain, a thrombospondin-1 repeat, a Cys-rich

domain, an ADAMTS spacer, seven additional thrombospondin-1 repeats. Furthermore, Zheng et al teach that VWFCP apparently is made as a zymogen that requires proteolytic activation, possibly by furin intracellularly. Further, sites for Zn^{2+} and Ca^{2+} ions are conserved in the protease domain. The Cys-rich domain contains an RGDS sequence that could mediate integrin-dependent binding to platelets or other cells. Alternative splicing gives rise to at least seven potential variants that truncate the protein at different positions after the protease domain. Alternative splicing can have functional significance, producing proteins with distinct abilities to interact with cofactros, connective tissue, platelets and von Willebrand factor (see abstract, Fig. 1, Fig. 1, and Fig. 3 in particular). Finally, Zheng et al teach that the characterization of the VWFCP (ADAMTS13) will facilitate the investigation of important biochemical and medical questions and can lead to the development of more specific treatment for TTP (see page 41062, last ¶ in particular).

The claimed invention differs from the reference teachings only by the recitation of an isolated antibody which specifically binds to the specific portion of ADAMTS-13.

However, it has been held that once the antigen of interest is selected, the use of that antigen in the known method of Kohler and Milstein will result in the expected hybrid cell lines and the specific monoclonal antibodies. Ex parte Erlich, 3 USPQ2d 1011, 1015 (BPAI 1986).

Campbell teaches that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (see page 3 figure 11.1 in particular). One field of research in which monoclonal antibodies may prove of particular value is in the study of chromosomal proteins. The search for those chromosomal proteins which are responsible for determining cell phenotype has been particularly long and comparatively fruitless and monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins. As hybridoma production becomes a more routine laboratory technique (see page 29 and 30 under Basic research in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to to make a monoclonal antibody as taught by Campbell against the polypeptides of SEQ ID NO: 1 taught by the Zheng et al reference.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it was customary at the time the invention was made to make monoclonals against any new macromolecule as taught by Campbell and to facilitate the investigation of important biochemical and medical questions which can lead to the development of more specific treatment for TTP taught by the Zheng et al reference.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 7/14/08, have been fully considered, but have not been found convincing.

Applicant did not address the rejection. Accordingly the rejection is maintained for reasons of records.

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 34 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-7 of copending Application No. 10/549317. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are expressly claiming the same subject mater, although they differ in scope. Specifically, pending claims 5-7 of the `317 application and instant claims are directed to antibodies capable of binding to a polypeptide or a peptide fragment derived from the ADAMTS-13 polypeptide.

This is a <u>provisional</u> obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 7/14/08, have been fully considered, but have not been found convincing.

Applicant submits that the mentioned claims 5 - 7 have "withdrawn" status in the '317 case and, hence, will not issue there. Since it remains to be seen when or even whether the common owner will pursue the subject matter of these withdrawn claims, applicant respectfully demurs on the issues of a terminal disclaimer. See MPEP 804, section B. 1 ("If 'provisional' ODP rejections in two applications are the only rejections remaining in those applications, [then] the examiner should withdraw the ODP rejection in the earlier filed application ...")

The Examiner notes that the withdrawn status of claims 5-7 in the`317 application means that the claims are still pending and not cancelled. Therefore, the rejection is proper. Regarding the MPEP 804 section B.1, the Examiner notes that the ODP is not the only rejection remaining in this application. Accordingly, the rejection is maintained.

18. Claims 35 and 37 are objected. Claim 38 is objected to because it depends from objected claim 35. Claims 34 and 36 are rejected.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 16, 2008

/Maher M. Haddad/
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